DETAILED DESCRIPTION

[Detailed Description of the Invention]
[0001]
[Field of the Invention]This invention relates to the anti-cataract agent which makes the lycopene an active principle.
[0002]
[Description of the Prior Art]As an anti-cataract agent used for prevention or the therapy of a senile or diabetic cataract, Now, pirenoxine eye drops, reduced glutathione eye drops, a salivary gland hormone lock, a tiopronin lock, and vitamins (for example, vitamin C, vitamin E, etc.) are used by clinical [actual] (Seiji Kumakura: chemicals economy, the November, 1993 item, 78-83 pages). However, these things do not have sufficient curative effect.
[0003]
[Problem(s) to be Solved by the Invention]There is SUBJECT of this invention in providing the anti-cataract agent which can demonstrate sufficient prevention or curative effect by instillation and administration to the cataract started as complication of senility or diabetes mellitus.
[0004]
[Means for Solving the Problem]As a result of inquiring wholeheartedly that this invention persons should attain said SUBJECT, lycopene, The knowledge of demonstrating sufficient provention or a curative effect by administration or instillation was carried out to the onset of a cataract of a streptozotocin derivation diabetes-mellitus model which is a cataract and a diabetic complication cataract model of ICR/f which are natural onset cataract models considered to be one of the senile cataract models. This invention is completed based on the knowledge. That is, this invention is an anti-cataract agent making lycopene into an active principle.
[0005]
[Embodiment of the Invention]The lycopene used for this invention shall also contain the plant bodies containing the inclusion of the substance concerned, for example, substance concerned, other than the substance concerned or those debris, the extracts produced by extracting from a plant body, or those refining things. The various mixtures of the lycopene or the mixture of the lycopene and its inclusion is also included. And those things shall not ask how of a manufacturing method. Here, it is shown still more concretely about the lycopene used for this invention. Although the lycopene used for this invention can also purchase the commercial lycopene (the product made by SIGMA, L9879), a publicly known chemical synthetic method (Hengartner, Urs; Bernhard, Kurt; Meyer, Karl; Englert, and Gerhard; --) [Glinz, Ernst and] Synthesis, isolation, and

NMR-spectroscopic characterization of fourteen(Z)-isomers of lycopeneand of some acetylenic didehydro- and tetradehydrolycopen es, extraction method from Helv. Chim. Acta and VOLUME6 PAGES:1848-65 (1992) or various plant bodies: 75 NUMBER: (Hakala, Sari H.; Heinonen, and I. --) [Marina and] ChromatographicPurification of Natural Lycopene, J. Agric. Food Chem. DATE: VOLUME: 42 NUMBER: 6 PAGES: It can obtain by 1314-16 (1994) etc.

[0006]In the case of a plant body extraction method, various kinds of plant bodies which contain the lycopene as extraction feed can be used, but it is points, such as safety, high-volume production capability, and refining cost, and especially a tomato is desirable. . [whether extracting processing of extraction feed or its debris is carried out using a solvent, and judgment refining of the obtained extract is further carried out with liquid chromatography etc., and] Or fabricating articles which used the plant body as the raw material, such as juice and a puree, are processed with the alternative adsorbent of a lycopene, this lycopene Type is condensed, and the lycopene is obtained by carrying out judgment refining of the concentrate with a countercurrent distribution method, liquid chromatography, etc. further.

[0007](Medication method) Prevention or the remedy agent of the cataract of this invention is suitably used in taking orally or parenterally for prevention of cataracts, such as senile cataract and diabetic cataract, and a therapy. Namely, of course depending on taking orally, a vein, and intraperitoneal administration, instillation also shows a remarkable curative effect.

[0008](Pharmaceutical-preparation-izing) It can prepare suitably by a method publicly known in any forms, such as liquids and solutions, such as solid preparations, such as a tablet, a granule, powder medicine, and a capsule, or ophthalmic solutions, and injections, as a gestalt of pharmaceutical preparation. Excipients, such as the binding material and disintegrator which are usually used, a thickener, a dispersing agent, a resorption accelerator, corrigent, a buffer, a surface-active agent, a solubilizing agent, a preservative, an emulsifier, an isotonizing agent, a stabilizing agent, and pH modifier, may be suitably used for these pharmaceutical preparation.

[0009]Although the dosage of the lycopene of this invention in the purpose of [dose (henceforth [this invention] dosage)] this invention changes with the kind, its pharmaceutical form and a patient's age, weight, shape of an indication, etc., For example, in the case of injections, it is [adult 1 time day / 0.01-50 mg] preferably good [several adult days and about 0.1-500 mg of single doses] in the case of about 0.1-10 mg and an oral administration agent to prescribe about 10-200 mg for the patient preferably. In the case of ophthalmic solutions, it is [0.01 to 5% (w/w) of concentration] preferably good for 1-2 drops per time to apply eyewash about 2 to 5 times preferably in the thing about 0.5 to 2% (w/w) in one to five days. Concomitant use combination may be carried out and making a lycopene independent contain as an active principle may make the anti-cataract agent of this invention contain other existing anti-cataract agents the thing of a non-theory, and there.

[0010]It experimented using the anti-cataract effect (experimental method) 8-week old to the natural onset cataract rat (ICR/f rat) of example of experiment 1 lycopene, the male, and the ICR/f rat (seven animal / group, the average weight of 190g). The control group which carried out free ingestion only of the MF powder feed similarly for the lycopene mixed feed group and comparison which added the lycopene (the product made by SIGMA, L9879) at a rate of 0.25% in MF powder feed (made by Oriental Yeast Co., Ltd.), and the rat was made to carry out free ingestion for four weeks was provided. Mydrin-P (made by Santan Pharmaceutical Co., Ltd.) performs anterior eye segment overview photography with the slit image of a lens after mydriasis during an experimental period weekly by NIKON zoom slit lamp microscope FS-3 (made by NIKON CORP.). In accordance with the method (the ophthalmology appropriate for ****, two volumes, No. 9, 1307-1312 pages, 1985) of Nishida and others, the stage classification was carried out in six steps of 0-5. The ICR/f rat used for the experiment is already the stage 3 (although nebula of a lens is not accepted macroscopically) at the time of an experiment start. slight turbidity is observed in the quality of back sac hypodermis by a slit image -- it is -- it was made with cataractogenesis the stage 4 nebula of a lens is macroscopically accepted to be with the time of lens turbidity

advancing during the experimental period, and the rate of cataractogenesis (%) was computed by the number of cataractogenesis eyes / the total number of eyes x100.

[0011](Experimental result) An experimental result is shown in Table 1. The control group accepted nebula of the lens more remarkable than the 15th day with progress of an experimental period, and the rate of cataractogenesis in the 21st day was 50%. On the other hand, by the lycopene administration group, the period when an onset rate is low continued for seven days from the 15th to the 21st compared with the control group.

[0012]

(日)	13	14	15	16	17	18	19	20	21	22
対照 (%)	0	0	7	7	21	36	43	43	50	50
リコペン投与群 (%)	0	0	0	7	7	7	7	29	36	50

[Table 1]Advance progress of the cataract of an ICR/f rat

[0013]Twelve example of experiment 2 (test method) diabetical rats were divided into every six-animal (A) control group and (B) lycopene (product [made by SIGMA], L9879) administration group (75 ppm of opposite feed), and were bred for 12 weeks, carrying out observation evaluation of the advancing state of the diabetic cataract daily in the meantime -- the check test of cataract depressor effect -- it carried out. Production of 1 diabetical rat and the check test of 2 cataract depressor effect were carried out by the following methods.

[0014]1) A method of producing a diabetical rat : 50 mg per weight of 1 kg was injected intraperitoneally for the streptozotocin (made by Sigma) with the conventional method to the Wis t a r system rat (a male, 10-week old, weight of 270g), and the diabetical rat was produced.

2) Japanese ** estimated the degree of nebula of the lens of a cataract depressor effect check test method rat in nine steps of 0-8.

Although turbidity takes place even to the center section of 4 -> lens surface where turbidity takes place even to the center section of 3 -> lens surface where air ball status change-ization takes place to 2 -> equator-lentis part from which air ball status change-ization takes place to 0-->-change-less 1 -> equator-lentis part a little a little, Turbidity spreads on the whole 5 -> lens surface which can be looked at through a fluoroscope, and the whole 8 -> lens in which the core of 7 -> lens to which nebula of the core of 6 -> lens which cannot see through eyegrounds, either takes place a little becomes cloudy whitens eyegrounds thoroughly.

A result is shown in Table 2. From the result of Table 2, it compares with contrast, the onset of the diabetic cataract is controlled, and it judges that a lycopene administration group is effective in the onset of the diabetic cataract, and prevention and the therapy of advance.

[0015]

[Table 2]Advance progress of the diabetic cataract of a diabetical rat

(日)	46	50	64	67	71
対照	0. 06±	3. 13±	4. 31±	4. 75±	5. 56±
	0. 25	2. 70	2. 68	2. 93	3. 37
リコピン投与 6		1. 08±	1. 75±	1. 92±	3. 58±
群		0. 29	1. 06	1. 24	1. 78

(Note 1) Marks : average value of the degree of nebula of the lens of the right and left of six rats[0016]Example of experiment 3 single-dose-toxicity-study (experimental method) 5-week old, a sex, a Crj:ICR mouse (the male mouse average weight of 27 g) Lycopene (product [made by SIGMA], L9879) 1 g/kg dissolved in the olive oil was respectively observed for 14 days after compulsive single time internal use to the sex mouse using the female mouse average weight of 22 g (five animal / group). The sex mouse was respectively medicated only with the olive oil in a similar manner as contrast. After the end of an experimental period, pathological anatomy of all the examples was performed and the existence of the abnormalities of whole body each organ was checked.
(Experimental result) There was no death animal at administration of the lycopene, and the sex mouse did not show clinical symptoms at all, but showed favorable weight increase during the experimental period. Abnormalities were not accepted at all by pathological anatomy of all the examples after the end of an experimental period.
[0017]
[Work example 1] -
The example 1 (oral-administration agent: tablet) of pharmaceutical preparation
It is milk sugar the 20 mg lycopene (the product made by SIGMA, L9879), 80mg starch 17mg magnesium stearate Not less than 3 mg was considered as 1 dose, and it tablet-ized with the conventional method.
[0018]
The example 2 (oral-administration agent: tablet) of pharmaceutical preparation
It is milk sugar the 50 mg lycopene (80% of purity, tomato extract), 80mg starch 17mg magnesium stearate Not less than 3 mg was considered as 1 dose, and it tablet-ized with the conventional method. the lycopene shown in this example of pharmaceutical preparation -- methods (Hakala, Sari H; Heinonen, and I. --), such as HAKARA, [Marina and] Chromatographic Purification of NaturalLycopene, J. Agric. Food Chem.DATE:VOLUME: 42 NUMBER: 6 PAGES: It prepared according to 1314-16 (1994).
[0019]
The example 3 (oral-administration agent: emulsified liquid agent) of pharmaceutical preparation
It is chain saturated fatty acid triglyceride 70mg tocopherol 1mg orange oil inside the 30 mg lycopene (the product made by SIGMA, L9879), 20 mg Deca glycerol monostearate 30 mg Glycerin Water is added to not less than 750 mg to make 100 ml. After-distribution emulsification was uniformly carried out with the conventional method, and the lycopene emulsified liquid agent of internal application was obtained.
[0020]

The example 4 (ophthalmic solutions: emulsified liquid) of pharmaceutical preparation
It is Tween 60 the 10 mg lycopene (the product made by SIGMA, L9879). 10mg boric acid 7mg sodium chloride 6mg methyl p-hydroxybenzoate 0.2 mg Chlorobutanol 3 mg was melted in water with the conventional method, emulsification was carried out, and it could be 100 ml. pH was with sodium hydroxide and was adjusted the pH to 6.0.
[0021]
[Effect of the invention]The anti-cataract agent of this invention has high safety, and the effect of prevention of diabetic nature or senile cataract or a therapy can use it advantageously highly.

[Translation done.]